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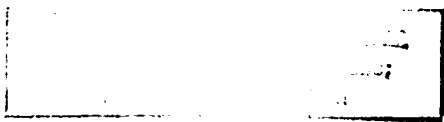
TECHNICAL REPORT

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TREATMENT OF TYPHOID AND PARATYPHOID FEVER
WITH NALIDIXIC ACID

By

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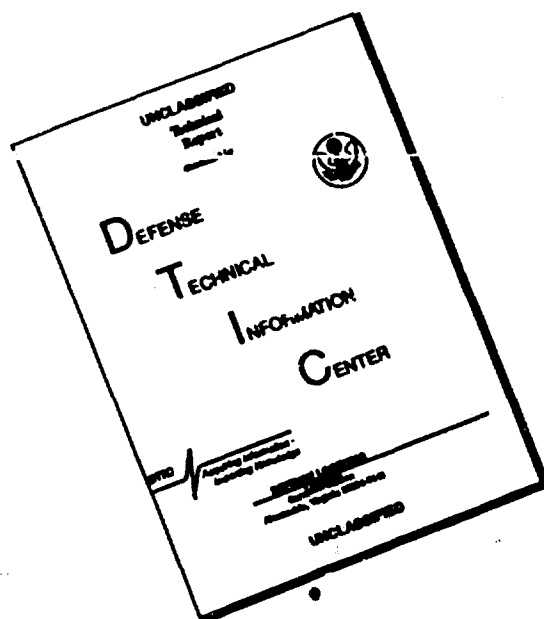
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13. ABSTRACT Thirty-two patients with proven typhoid or paratyphoid fever were studied clinically and bacteriologically and treated with nalidixic acid, 60 to 100 mg per kilogram body weight daily for 10 days. Twenty-eight out of 32 patients were cured. The average period for the patients to become afebrile was 9.5 days. No side-effects of therapy were noted			

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TREATMENT OF TYPHOID AND PARATYPHOID FEVER WITH NALIDIXIC ACID*

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Nalidixic acid (Negram) is a new anti-bacterial agent which is particularly effective against gram negative organisms. Barlow (1963), Lishman and Swinney (1963), and Thompson and Rae (1964) confirmed the effectiveness of nalidixic acid against the great majority of proteus and *E. coli* strains, the organisms most frequently encountered in urinary tract infections. Moorhead and Parry (1965) proved its effectiveness in the treatment of Sonne dysentery.

This paper reports the results of treatment of 32 patients with proven acute typhoid or paratyphoid infections with nalidixic acid.

Materials and Methods

Thirty-two patients with the typical clinical picture of acute typhoid or paratyphoid fever were admitted to the Government Fever Hospital, Abbassia, Cairo, from May to September 1968.

None of the patients had previously received antibiotic treatment. On admission, laboratory examinations included white cell counts, urine and stool examinations for ova and parasites, and blood smears for malaria. Blood samples for culture and sensitivity and Widal agglutinations were taken on admission and at weekly intervals. Urine and stool cultures were made on admission and repeated three times on alternate days before discharging the patients from the hospital. Patients were followed-up for one month after discharge. Criteria for inclusion in the study were positive blood cultures for typhoid or paratyphoid organisms or positive stool or urine cultures plus a significant rising Widal titre. The time range from the onset of illness to the start of treatment varied from five to 11 days. Nineteen patients were males and 13 females. Their ages ranged from three to 45 years.

Two schedules of nalidixic acid treatment were followed, the first group (12 cases) was given the drug in dosage of 60 mg per kilogram body weight daily divided into six hourly doses. The second group (20 cases) was given the drug in dosage of 100 mg per kilogram body weight divided into six hourly doses. Treatment was continued in both groups until the patient became afebrile and then continued for an additional seven days. Treatment was considered a failure if the patient showed no response to treatment, the elevated temperature and toxicity remaining in spite of 10 days of treatment.

Results

Table I shows the distribution of our cases according to the method of diagnosis. Nineteen patients had positive blood cultures for typhoid and paratyphoid organisms and 13 cases had either positive stool or urine cultures in addition to a significantly rising Widal titre. The majority of the patients were adolescents in the age group 10 to 15 years. Table II summarises our results of treatment.

All initial positive blood, urine, and stool cultures were sensitive *in vitro* to nalidixic acid.

In the group of patients receiving the drug in dosage of 60 mg per kilogram body weight daily a general improvement occurred after an average of 5.5 days and normalization of temperature after an average of 10 days. In the group of patients receiving the drug in dosage of 100 mg per kilogram body weight daily,

* Nalidixic acid was kindly given to us by Winthrop Company as "Negram"

The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Egyptian Ministry of Public Health, the Navy Department, or the Naval Service at large.

TABLE I. METHOD OF DIAGNOSIS.

Organisms	Positive Blood Culture	Positive Stool Culture Plus Significant Widal Titres
Typhoid	13	10
Paratyphoid - A	6	1
Paratyphoid - B	-	2
Total	19	13

general improvement occurred after an average of five days and normalization of temperature after an average of nine days. Three cases were considered as treatment failure since their general condition deteriorated in that they became more toxic and they remained febrile after 10 days of nalidixic acid treatment. They promptly responded to chloramphenicol treatment.

Normalization of temperature bore no relation to the duration of the disease prior to therapy.

One typhoid patient relapsed clinically and bacteriologically after seven days of stoppage of nalidixic acid in dosage of 60 mg per kilogram body weight daily; the patient responded to five days chloramphenicol treatment in dosage of 50 mg per kilogram body weight daily.

No significant side-effects of nalidixic acid therapy were noted in this study. Typhoid complications such as haemorrhage, perforation or development of the carrier state were not noted in this series.

Discussion

Taneja and Ghai (1957), Chakrabhorthy (1961), Ikeme and Aman (1966), and Omar and Wahab (1967) found that the wide use of chloram-

phenicol in the treatment of typhoid or paratyphoid fever appears to have led to the appearance of resistant *Salmonella* strains with resultant lack of response to therapy. Also the persistent occurrence of relapses, complications, development of chronic carriers, and chloramphenicol-associated drug complications demanded a continuous search for better drugs.

Robertson, *et al.* (1968) found ampicillin to be effective in the treatment of acute typhoid and paratyphoid fever in 77 per cent of cases. No report, however, appeared on the use of nalidixic acid in the treatment of acute typhoid and paratyphoid fever. In our study 28 (87.5 per cent) of 32 patients treated with nalidixic acid were cured clinically and bacteriologically, three patients failed to respond to treatment and one patient relapsed. The average time for the temperature to return to normal was 9.5 days. There was no significant statistical difference in response between the two treatment schedules (60 or 100 mg per kilogram body weight daily). No side-effects were noticed during nalidixic acid treatment. Though the response to nalidixic acid is slow we still think that it can be used as an alternative drug to chloramphenicol in the treatment of acute typhoid or paratyphoid fever particularly in those patients who also have a urinary tract infection, and when chloramphenicol is unavailable or contra-indicated.

Summary

Thirty-two patients with proven typhoid or paratyphoid fever were studied clinically and bacteriologically and treated with nalidixic acid, 60 to 100 mg per kilogram body weight daily for 10 days. Twenty-eight out of 32 patients were cured. The average period for the patients to become afebrile was 9.5 days. No side-effects of therapy were noted.

TABLE II. RESPONSE TO THERAPY.

Schedule of Therapy	Number of Cases	General Improvement (Days)		Normalization of Temperature (Days)		No. Drug Failures	No. Relapses
		Range	Average	Range	Average		
60 mg.	12	4-8	5.5	6-14	10	1	1
100 mg.	20	3-9	5	5-13	9	2	0

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